Med. J. Cairo Univ., Vol. 90, No. 7, December: 2099-2111, 2022
www.medicaljournalofcairouniversity.net

Serial Assessment of Diaphragmatic and Peripheral Muscles Thickness and their Impact on Discontinuation of Mechanical Ventilation

MOHAMED EL GHOBASHY, M.D.*; AHMED S. AWAD, M.D.*; AHMED YEHIA MOHAMED, M.Sc.**; YASSER NASSAR, M.D.** and MOHAMED FAKHER, M.D.**

The Departments of Diagnostic Radiology and Critical Care Medicine Diagnostic Radiology** , Faculty of Medicine, Cairo University*

Abstract

Background: Diaphragmatic weakness is common among patients undergoing mechanical ventilation and is considered a contributing factor in weaning failure. Recent studies have proposed that the ventilator is one of the causes of decreased diaphragm force-generating capacity seen in mechanically ventilated patients. On the other hand, myopathy is a common complication of ICU stay and may delay mechanical ventilation weaning. The study was focused on detecting the changes of both diaphragmatic and quadriceps muscles in different modes of mechanical ventilation by ultrasound and considering diaphragm thickness and excursion as a predictor of weaning outcome.

Aim of Study:

- Detection of the daily effects of invasive mechanical ventilation on both diaphragmatic and quadriceps muscles thickness by ultrasound
- Comparing the effect of controlled versus spontaneous modes of ventilation on diaphragmatic thickness, excursion, and quadriceps muscle thickness by ultrasound.

Patients and Methods: This study included 50 invasively mechanically ventilated patients. Diaphragmatic thickness (DT), diaphragmatic excursion (DE), and quadriceps muscle thickness were measured every 48 hours starting from the first day of mechanical ventilation.

Results: Patients on spontaneous modes of mechanical ventilation showed higher values of DT (on days 4 and 8) and DTF (on days 2, 6, and 10) compared to patients on controlled modes. Also, patients with successful weaning showed higher values of DTF (on days 0 and 8) and DE (on days 2 and 8) than those with failed weaning. The changes in diaphragmatic functions had occurred as early as the first days of mechanical ventilation. The receiver operator characteristic (ROC) curves showed cut-off points for successful weaning of 0.33 and 19mm for DTF and DE, respectively. Quadriceps muscle showed a daily decrease in thickness regardless of the mode of ventilation, and there was no correlation with either DTF or DE.

Conclusion: There was a continuous decline of DT and DTF among patients on controlled modes of mechanical ventilation compared to spontaneous modes. Also, there was a continuous decline in DTF and DE among patients with failed weaning compared to patients with successful weaning.

Key Words: *Diaphragm – Quadriceps muscle – Ultrasound – Mechanical ventilation.*

Correspondence to: Dr. Mohamed El Ghobashy
E-Mail: Mohamed.elghobashy@CU.edu.eg

Introduction

MECHANICAL ventilation is one of the common procedures in critical care. Weaning from mechanical ventilation (MV) is one of the most frequently encountered challenges in modern ICUs. An estimated 20% of mechanically ventilated patients face failed extubation (requiring reintubation within 48h of extubation) **[1]**.

One of the significant determinants of weaning failure is the imbalance between the mechanical load imposed on the diaphragm and its ability to cope with it. Hence, evaluating diaphragmatic function before any weaning attempt could be of importance. There is growing evidence that diaphragmatic dysfunction plays a fundamental role in ventilator dependency **[2,3]**.

Bedside ultrasonography (US) can help evaluate and manage mechanically ventilated patients. In intensive care units, the role of ultrasound is not only to diagnose but can be used as a guide for managing mechanical ventilation from the beginning to weaning. To obtain a comprehensive functional of critical care patients during mechanical ventilation **[2]**.

Bedside neuromuscular US is an accessible and noninvasive method that can be used to quantify skeletal muscle thickness **[4,5]**. Combining diaphragmatic and peripheral muscles ultrasound can be helpful in the detection of muscle atrophy impairing weaning.

Detect the impact of diaphragmatic thickness fraction and diaphragmatic excursion on weaning from mechanical ventilation.

Thickness and echogenicity of the diaphragm can be assessed using B-mode ultrasound, also known as real-time imaging. M-mode ultrasound, which displays a single beam of a B-Mode image on the y-axis as it changes over time on the x-axis, evaluates a specific site over time and can assess excursion [6].

During ICU stay, a significant proportion of the mechanically ventilated ICU patients develop marked muscle wasting and weakness of limb muscles due to acquired myopathy, neuropathy, or a combination of both, leading to delayed recovery, with subsequent increased morbidity, financial costs, and decreased quality of life The ICU-acquired neuromuscular disorder increase with the duration of critical illness and abnormalities begin to develop early in the hospital course [7].

Van den Berghe et al., used multivariate analysis and found that the reduction in electrophysiologically diagnosed neuromuscular abnormalities was independently associated with a reduction in prolonged mechanical ventilation [8].

Muscle ultrasound is a reliable technique to visualize normal and pathological muscle tissue. Neuromuscular disorders can lead to structural muscle changes that can be adequately assessed with ultrasound: Atrophy can be objectified by measuring muscle thickness, while infiltration of fat and fibrous tissue increase muscle echo intensity [9].

Patients and Methods

The study is a prospective observational study on adult patients admitted to the Critical Care Medicine Department of Cairo university hospital over six months starting from Septeber 2017 to Feb. 2018. The study was approved by the Medical Ethics Committee of the Faculty of Medicine.

Inclusion criteria: All adult patients who required invasive mechanical ventilation were enrolled in the study after obtaining informed written consent from the patient's next of kin or legal guardians before conducting the study regarding participation and publication of the study.

Exclusion criteria:

1- Inability to obtain proper acoustic windows.

2- Inability to obtain written informed consent.

3- Patients known to have diaphragmatic paralysis.

4- Patients known to have neuromuscular disorders, for example, Guillain Barre Syndrome and Myasthenia gravis.

5- Patient on neuromuscular paralyzing agents.

6- Patients below 18 years and pregnant females.

All patients were subjected to the following:

1- Detailed history taking.

2- Complete physical examination: Detailed clinical examination of all patients, including assessment of the vital signs [Heart rate (ER), respiratory rate (RR), oxygen saturation (S02), and temperature (Temp)].

3- Laboratory investigations:
- Complete blood count (CBC).
- Coagulation profile: Prothrombin time (PT), Prothrombin concentration (PC), and International normalized ratio (INR).
- Arterial blood gases (ABGs).
- Liver functions: Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), and bilirubin (total and direct).
- Kidney functions: Sodium (Na), Potassium (K), serum Creatinine (Creat.) and blood Urea (BUN).
- Random blood sugar.

4- Bedside twelve leads Electrocardiogram (ECG) and chest X-ray (CXR).

5- Ultrasonography:

Ultrasound measurements were taken immediately after connecting the patient to mechanical ventilation and then repeated every 48 hours for a total of five consecutive measurements: The first measurement on day 0 Second measurement on day 2 Third measurement on day 4, the Fourth measurement on day 6, Fifth measurement on day 8 Sixth measurement on day 10.

Measurements:

- Diaphragmatic thickness, diaphragmatic thickness fraction (DTF), and quadriceps muscle thickness were measured during controlled and spontaneous modes of mechanical ventilation, while diaphragmatic excursion (DE) was measured during spontaneous modes only.

- Patients were kept in a supine position with head at zero level.
- Measurements were done using an ultrasound unit and digital ultrasonic imaging system TOSHIBA XARIOG100.

Ultrasound examination technique:

1- *Diaphragmatic thickness (DT):*

- The diaphragm was visualized by placing the 10MHz linear probe over the lateral chest wall, in the sagittal orientation opposite the eighth to ninth intercostal space, almost midway between the anterior axillary and mid axillary lines, to visualize the diaphragmatic muscle 1 to 2cm below the costophrenic recess (Fig. 1).
- The diaphragm was imaged as a structure with three distinct layers (Figs. 2,3), two parallel hyperechoic lines (the pleura and the peritoneal membrane), and a hypoechoic structure between them (the muscle itself) [10].
- Different measures were taken for diaphragmatic thickness, and the mean value was calculated.
- A diaphragm thickness <0.2cm, measured at the end of expiration, was suggested as the cut-off to define diaphragm atrophy [11].

Fig. (1): Linear probe positioned between anterior and mid-axillary lines perpendicular to the chest wall.

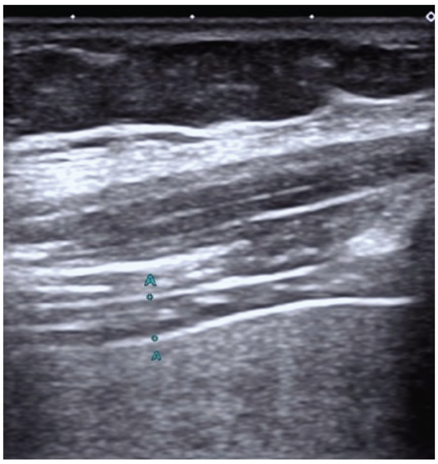

Fig. (2): Ultrasound measurement of diaphragmatic thickness.

Fig. (3): Subcostal position of the ultrasound probe.

2- *Diaphragmatic thickness fraction (DTF):*

Can be calculated from the formula:

$$\frac{\text{DT at the end of inspiration} - \text{DT at the end of expiration x 100}}{\text{Thickness at the end of expiration}}$$

Diaphragmatic excursion:

- At the Anterior axillary line in the subcostal region, a 2- to 4-N/1Hz convex probe (119) is directed medially, cranially, and dorsally (Fig. 3).
- B mode to was used to assess excursion, and M mode to measure the range of motion from the resting expiratory position to fullinspiration (normal range in adults 1.9 to 9cm) (Fig. 4).
- Excursion >2.5cm in adults cut off for excluding severe diaphragm dysfunction.

4- *Quadriceps muscle thickness:*

- A liner probe was placed midpoint between the anterior superior iliac spine and the superior aspect of the patella.
- Thickness was recorded as the distance between the femur and the posterior border of the fascia lata (Fig. 5).
- To ensure consistency, the patient's legs were extended and in a neutral position before each ultrasound examination.

5- The whole ultrasound examination was accomplished in 15 minutes.

Outcome parameters included:

- Successful weaning is defined as a state in which a patient could maintain his or her own breathing for 48 hours without ventilator support.
- Primary weaning failure: Defined as requirement for mechanical ventilation within 48 hours of self-breathing.
- Secondary weaning failure: Defined as the requirement for mechanical ventilation after successful weaning.

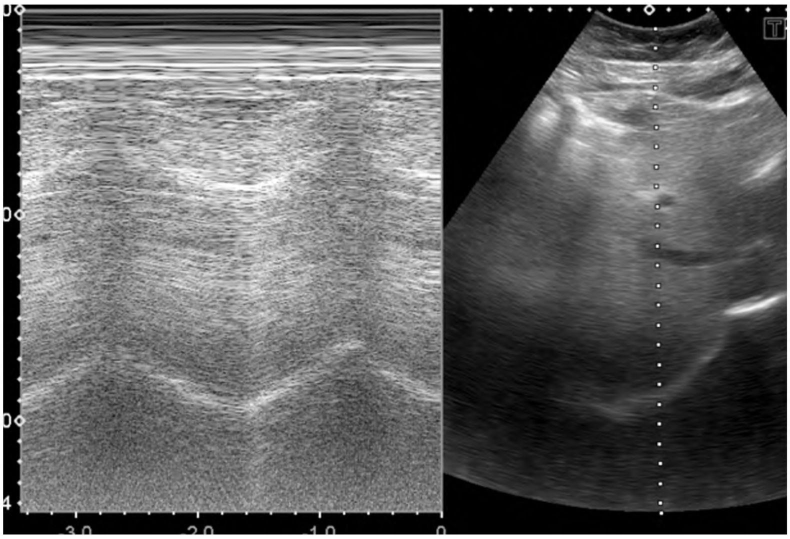

Fig. (4): Measurement of Diaphragmatic excursion using M mode.

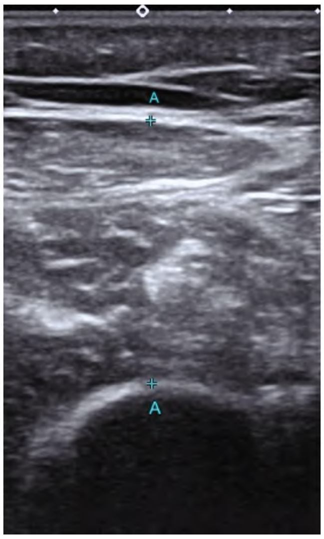

Fig. (5): Measurement of quadriceps muscle thickness in the transverse plane.

Statistical methods:

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were made using the non-parametric Kruskal-Wallis and Mann-Whitney tests. ROC curve was constructed with the area under curve analysis performed to detect the best cut-off value of TF for detection of successful extubation. *p*-values less than 0.05 are considered statistically significant.

Results

Our study included 50 mechanically ventilated patients admitted to the Critical Care Department Kasr El-Ainy University Hospital during the period from 1 September 2017 to 28 February 2018.

Descriptive data of the whole study population:

1- Age:

The age of the studied patients ranged from 22 to 85 years, with a mean of 53.6±20 years.

2- Gender:

Thirty (60%) of the studied patients were females, and 20 (40%) were males.

3- Cause of mechanical ventilation:

Twenty (40%) patients were ventilated due to parenchymatous lung diseases, 17 (34%) patients due to central nervous system causes (e.g. disturbance of consciousness level, 6 (12%) patients due to airway diseases, and 7 (14%) patients due to cardiac causes.

4- Comorbidities:

Thirteen (26%) of the studied patients had ischemic heart disease, 13 (26%) patients had diabetes, 18 (36%) patients had renal impairment, 16 (32%) patients were hypertensive, 4 (8%) patients had cerebrovascular strokes (CVS), and 10 (20%) patients had liver impairment.

5- SOFA score and APACHE 11 score:

- The average value of SOFA score was 6.6±4.1.
- The average value of APACI-IE Il score was 15.8±10.

6- Mode of mechanical ventilation:

Twenty (40%) patients were on pressure support ventilation and 30 (60%) patients were on controlled ventilation [25 (50%) patients were on volume control and 5 (10%) patients were on pressure control].

7- Days of mechanical ventilation:

The mechanical ventilator days ranged from 3 to 17 days, with a mean value of 6.6 days ± 3.75 days.

8- Length of hospital stay:

The length of ICU stay ranged from 6 to 25 days with a mean value of 11.66 days ± 3.94 days.

9- Weaning outcome:

Twenty-six (52%) patients were weaned successfully, while 24 (48%) patients failed to wean (Table 1).

Table (1): Outcome from mechanical ventilation.

	Number (%)
Outcome:	
Successful weaning	26 (52%)
Failed weaning	24 (48%)

SOFA score mean ± SD was lower in patients with successful weaning, 5.12±3.25 versus failed weaning, 8.3±4.4 (*p* 0.009).

10- *Evaluation of diaphragmatic thickness by ultrasound:*

Ultrasound measurements were taken immediately after connecting the patient to mechanical ventilation and repeated every 48 hours for five consecutive measures (days 0,2,4,6,8 and 10).

Inspiratory diaphragmatic thickness (DTi):

DTi mean ± SD on day O was 3.21±0.73mm, day 2 3.18±0.75mm, day 4 3.12±0.78mm, day 6 3.01±0.85mm, day 8 2.81±0.44mm and day ten 2.8±0.26mm.

DTi showed a significant daily decline on days 6-8 [–3.3%/day, *p* 0.0451. Other days showed statistically non-significant changes days 0-2 was [–0.45%/day, *p* 0.48], days 2-4 [–0.9%/day, *p* 0.53], days 4-6 [–1.7%/day, *p* 0.854] and days 8-10 [–0.1%/day, *p* 0.95], (Table 2).

Table (2): DTi for the entire study group.

	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10
Mean SD	3.21 ±0.73	3.18 ±0.75	3.12 ±0.78	3.01 ±0.85	2.81 ±0.44	2.8 ±0.26

On spontaneous ventilation (PS):

DTi showed a significant daily increase on days 2-4 [0.1%/day, *p* 0.0051 and on days 6-8 [0.3% /day, *p* 0.0161].

Other days showed statistically non-significant changes (*p*>0.05) on days 0-2 [0.3%/day, *p* 0.129], days 4-6 [0% /day, *p* 0.065], and days 8-10 [0.2% /day, *p* 0.90] .

On controlled ventilation (CMV):

DTi showed a daily decline on days 0-2 [–0.9% /day, *p* 0.0041 and days 6-8 [–4.5% /day, *p* 0.05].

Other days showed statistically insignificant changes on days 2-4[-1.7%/day, *p* 0.884], days 4-6 [–0.3%/day, *p* 0.059], and days 8-10 [–0.1%/ day, *p* 0.68].

DTi in PS versus CMV:

DTi mean ± SD was lower on day 4, 3.09mm± 0.86 versus 3.15mm±0.69 (*p* 0.019), and on day 8, 2.72±0.48mm versus 3±0. Imm (*p* 0.014) in CMV versus PS, respectively.

Other days showed statistically non-significant changes (*p*>0.05) (Table 3).

Table (3): DTi in patients on PSV and CMV.

	Spontaneous modes		Controlled modes		*p*-value
	Mean	SD	Mean	SD	
Day 0	3.12		3.26		0.055
Day 2	3.14		3.20	±0.82	0.905
Day 4	3.15	±0.69	3.09	±0.86	0.019
Day 6	3.15	±0.29	3.07		0.609
Day 8	3.18	±0.010	2.72		0.014
Day 10	3.22	±0.016	2.70	4:0.23	0.200

B- *Expiratory diaphragmatic thickness (DTe):*

DTe mean±SD on day 0 was 2.18 ±0.43mm, day 2 2.16 ±0.45mm, day 4 2.14±0.47mm, day 6 2.03±0.44mm, day 8 1.99±0.27mm and day 102.1± 0.19mm.

DTe showed a significant daily decline on days 4-6 [–2.5%/day, *p* 0.041].

Other days showed statistically non-significant changes days 0-2 [-0.45%/day, *p* 0.65], days 2-4 [–0.45%/day, p 0.69], days 6-8 [–0.9%/day, *p* 0.245] and days 8-10 [2.7%/day, *p* 0.89], (Table 4).

Table (4): DTe for the entire study group.

	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10
Mean SD	2.18 ±0.43	2.16 ±0.45	2.14 ±0.47	2.03 ±0.44	1.99 ±0.27	2.1 ±0.19

On PS ventilation:

DTe showed statistically significant daily increase on days 2-4 [1.6%/day, *p* 0.0171 and days 6-8 [2%/day, *p* 0.0151.

Other days showed statistically non-significant changes on days 0-2 [0.47%/day, *p* 0.358], days 4-6 [1.1% /day, *p* 0.655], and days 8-10 [1.28% [day, *p* 0.99].

On CMV:

DTe showed a significant daily decline on days 0-2 was [–1.1% /day, *p* 0.0191 and days 2-4 [–1.7% /day, *p* 0.051].

Other days showed statistically non-significant changes days 4-6 [2.1% /day, *p* 0.135], days 6-8 [2%/day, *p* 0.257] and days 8-10 [0.5%/day, *p* 0.564].

DTe in CMV versus PS ventilation:

DTe mean ± SD was lower on day 4, 2.08± 0.47mm versus 2.2±0.48mm L (*p* 0.017), and on day 8, 1.92mm±0.28 versus 2.34mm±0.1 (*p* 0.028) in CMV versus PS ventilation respectively.

Other days showed statistically non-significant changes (*p*>0.05), (Table 5).

Table (5): DTe in spontaneous and controlled modes of MV.

	Spontaneous modes		Controlled modes		*p*-value
	Mean	SD	Mean	SD	
Day 0	2.11	±0.46	2.23	:kO.41	0.166
Day 2	2.13	4:0.49	2.18		0.136
Day 4	2.20	±0.48	2.08	±0.47	0.017
Day 6	2.25	±0.12	1.99	±0.51	0.117
Day 8	2.34	±0.10	1.92		0.028
Day 10	2.40	15	1.900	±0.23	0.800

C- *Diaphragmatic thickness fraction (DTF):*

DTF mean ± SD on day 0 was 47.08±30.3%, day 2 was 47.43±1 day 4 was 45.52 ±19.22%, day 6 was 47.57±23.41%, day 8 42.50±23% and day 1037±4.1%.

DTF showed a significant daily increase on days 4-6 [2.25%/day, *p* 0.028) and significant daily decrease on days 6-8 [–5.1%/day, *p* 0.0361.

Other days showed statistically non-significant changes on days 0-2 [0.27%/day, *p* 0.358], days 2-4 [–2%/day, *p* 0.17], and days 8-10 [-5.8%/day, *p* 0.69], (Table 6).

Table (6): DTF for the total study group.

	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10
Mean%	47.08	47.34	45.52	47.57	42.50	37.40
SD%	±20.38	±19.48	±19.22		±23.09	±4.10

In patients with successful weaning:

DTF showed a significant daily increase on days 6-8 [5.4%/day, *p* 0.0151].

Other days showed statistically non-significant changes on days 0-2 [1.55%/day, *p* 0.358], days 2-4 [–2.1%/day, *p* 0.17], days 4-6 [–6%/day, *p* 0.613], and days 8-10 [2%/day *p* 0.137].

In patients with failed weaning:

DTF showed a significant daily decrease on days 6-8 [–5.1%/day, *p* 0.0371 and days 8-10 [–3.1 %/day, *p* 0.0151] .

Other days showed statistically non-significant changes [on days 0-2 was 3.02%/day (*p* 0.358), days 2-4 0.35% [day (*p* 0.51), days 4-6 4.5%/day (*p* 0.2980)].

DTF in patients with failed versus successful weaning:

DTF mean ± SD was lower on day 0 [39.29%± 14.7 versus, *p* 0.0141], on day 2 [41.67±17.32% versus 52.58±20.22%, *p* 0.0471] and on day 8 [41±19.99% versus 49±5.25%, *p* 0.0411] in patients with failed versus successful weaning respectively.

Other days showed statistically non-significant changes (*p*>0.05) (Table 7).

Table (7): DTF for patients with successful and failed weaning.

	Successful weaning		Failed weaning		*p*-value
	Mean	SD	Mean	SD	
Day 0	54.27	±22.44	39.29	± 14.70	0.014
Day 2	52.58	±20.22	41.67	±17.32	0.047
Day 4	50.28	±20.75	41.96		0.263
Day 6	44.20	±28.96	48.50	±22.53	0.691
Day 8	49.00	±5.25	41.00		0.041
Day 10	51.00		31.67		0.700

On PS Ventilation:

DTF showed a significant daily increase on days 0-2 [15%/day, *p* 0.0311], days 6-8 [6.7%/day, *p* 0.17], and on days 8-10 [8%/day, *p* 0.039].

Other days showed statistically non-significant changes on days 2-4 [–1.9%/day, *p* 0.658], on days 4-6 [2.7%/day, *p* 0.17].

On CMV:

DTF showed a significant daily decrease on days 0-2 [–13%/day, *p* 0.121], and days 4-6 [7.1% /day, *p* 0.022].

Other days showed statistically non-significant changes days 2-4 [2%/day, *p* 0.43 11, days 6-8 [5%/day, *p* 0.233] and days 8-10 [–0.7%/day, *p* 0.752].

DTF in PSVversus CMV:

DTF mean ± SD was higher on day 2 [46.4± 15.63% versus 10.82%, *p* 0.0341], on day 6 [40.5± 12.29% versus 36.87±14.98%, *p* 0.0461] and on day 10 [54.23±26.16% versus 42.7±19.23%, *p* 0.021] in patients on PSV versus CMV respectively.

Other days showed statistically non-significant changes (p>0.05) (Table 8).

Table (8): DTF on PSV versus CMV.

	Spontaneous modes		Controlled modes		p-value
	Mean	SD	Mean	SD	
Day 0	35.12	±15.63	46.26	±15.80	0.655
Day 2	46.40	±20.67	39.29	±10.82	0.034
Day 4	38.45	±10.69	42.09		0.719
Day 6	40.50	±12.29	36.87	±14.98	0.046
Day 8	45.98	±18.10	43.48		0.514
Day 10	54.23	±26.16	42.70	19.23	0.021

DTF in different causes of mechanical ventilation:

DTF mean ± SD was highest among patients with cardiac diseases 68.75±10.01 followed by parenchymatous lung disease 52.91±21.01, then neurological causes 31.14 ±20.51 and it was lowest among patients with airway diseases 19±5.03% (p 0.038) on day 6.

On day 8, DTF mean ± SD was highest among patients with parenchymatous lung diseases, 55.40±18.82%, while it was lowest among patients with the central nervous system (CNS) causes, 21±6.93% (p 0.023).

11- *Evaluation of diaphragmatic excursion (DE) bp M-mode ultrasound:*

DE mean ± SD on day 0 was 14±7.17mm; Day 2, 20.28±6.61mm; Day 4, 20.17±7.19mm. Day 6 19.94±7.2mm, Day 8 16.5±6.35mm, and Day 1017.4±0.55mm

DE showed a significant daily increase on days 0-2 [3mm/day, p 0.0381. Other days showed statistically non-significant changes [days 2-4 [–0.2mm/day, p 0.39], days 4-6 [–0.5mm/day, 0.655], days 6-8 [–1.7mm/day, p 0.157] and days 8-10 [0.45mm [day, p 0.99)], (Table 9).

Table (9): DE for the entire study group.

	Day 0	Day 2	Day 4	Day 6	Day 8	Day 10
Mean	14.01	20.28	20.17	19.94	16.5	17.40
SD	±7.17	±6.61	±7.19	±7.20	±6.35	±0.55

In patients with successful weaning:

DE mean ± SD showed a significant daily increase on days 0-2 [5.2mm/day, p 0.012) and on days 8-10 [1mm/day, p 0.0251.

Other days showed statistically non-significant changes days 2-4 [0.5mm/day (p 0.58), days 4-6 [-1.2mm/day, p 0.235], days 6-8 [0.2mm/day, p 0.89)].

In patients with failed weaning:

DE mean ± SD showed a significant daily decline on days 6-8 [-2.6mm/day, p 0.049).

Other days showed statistically non-significant changes days 0-2 [0.8mm/day, p 0.335], days 2-4 [0.92mm/day, p 0.258], days 4-6 [0.9mm/day, p 0.138], and days 8-10 [0.3mm/day, p 0.525].

DE in patients with successful versus failed waning:

DE mean ± SD on day 2 was highest at 21.83 mm±6.18 versus 15.86±6.13mm (p 0.048) and on day eight was 18±2.22mm versus 15±1mm (p 0.033) among patients with successful versus failed weaning respectively. Other days showed statistically non-significant changes (p>0.05).

ROC curve was measured for diaphragmatic thickness fraction and excursion for prediction of weaning (Fig. 6):

DTF:

The optimal cut-off point of DTF for weaning success was 0.33 with a sensitivity of 88.3% and a specificity of 78% and (p 0.026).

The area under curve [AUC] was 0.65 (95% confidence interval 0.36 to 0.8).

DE:

The optimal cut-off point of DE for weaning success was 19mm at the end of inspiration with a sensitivity of 82% and a specificity of 74% and (p 0.046) AUC was 0.54 (95% confidence interval 0.34 to 0.74) (Table 10).

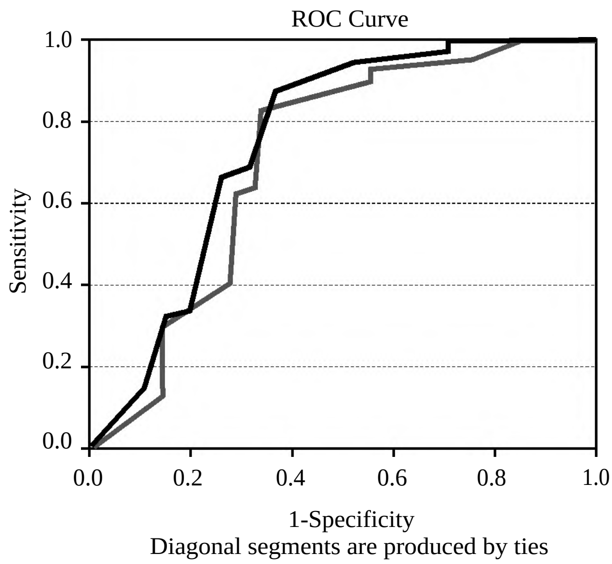

Fig. (6): ROC curve for DTF and DE.

Table (10): Values of Roc curve for DTF and DE.

Test Result	AUC	p-value	95% Confidence Interval		Sen-sitivity	Spe-cificity
			Lower Bound	Upper Bound		
DTF	0.705	0.026	0.36	0.805	88.3	78
DE	0.655	0.046		0.741	82	74

12- *Quadriceps muscle thickness:*

Quadriceps thickness mean ± SD on day 0 was 11.91±3.64mm; on day 2, 11.38±3.49mm; on day 4, 10.88±3.53mm. Day 6, 10.7±3.23mm; day 8, 10.68±2.5mm and day 10, 10.4±2.67mm.

Quadriceps thickness showed a significant daily decline on days 0-2 was 2.2%/day (*p* 0.019) and days 8-10 [1.3%/day, *p* 0.0261] (Fig. 7).

Other days showed statistically non-significant changes [on days 2-4 –2.2%/day (*p* +0.055) days 4-6 [–0.8%/day, *p* 0.245], days 6-8 [–0.1%/day, *p* 0.78].

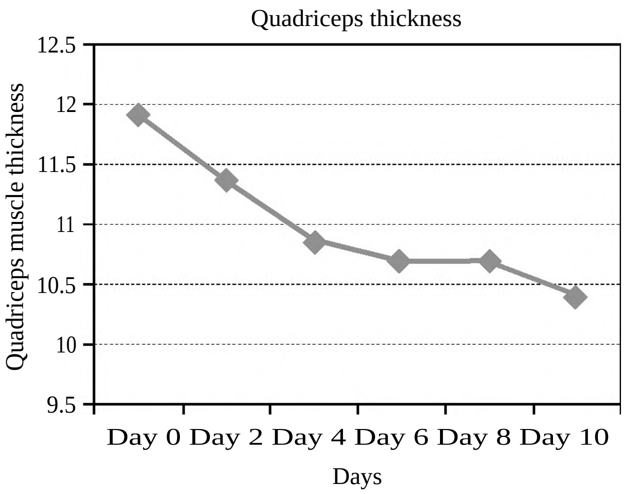

Fig. (7): Quadriceps muscle thickness for the total study group.

Discussion

Mechanical ventilation is a common procedure in critical care, and weaning from mechanical ventilation represents one of the most encountered challenges [1]. An estimated 20% of mechanically ventilated patients face failed extubation, and about 40% of the total ventilatory time is consumed in weaning trials [12].

Many mechanically ventilated ICU patients develop muscle wasting and weakness of diaphragmatic and skeletal muscles (such as the quadriceps femoris muscle) due to acquired myopathy, neuropathy, or a combination of both, leading to increased morbidity and difficult weaning from MV [8,13]. Risk factors that are incriminated in ICU-acquired myopathy are frequently encountered in ICU as sepsis [14], neuromuscular blocking agents [15,16], hyperglycemia, corticosteroids [17], and immobilization [18]. Mechanical ventilation itself may decrease the force of diaphragmatic contractions [19] which may contribute to difficult weaning [20].

One of the significant determinants of weaning failure is the imbalance between the imposed mechanical load and the diaphragmatic muscle power [2,3] hence the evaluation of diaphragmatic function before any weaning attempt could be vital to predicting the weaning outcome. Recently, diaphragmatic ultrasonography (US) has been introduced as a simple, noninvasive method for the evaluation of diaphragmatic and skeletal muscle [4,21] contractile activity [22] either by assessment of diaphragm excursion (DE) [20,23] or diaphragmatic thickness (DT) and thickness fraction (DTF) [24].

Combining diaphragmatic and quadriceps femoris muscle ultrasound can help detect the presence and the progression of atrophy of the diaphragm and quadriceps femoris muscles.

This study primarily aimed to detect invasive mechanical ventilation's daily effects on diaphragmatic and quadriceps muscle thickness by ultrasound. Our secondary aim was to compare the impact of controlled versus spontaneous ventilation modes on the diaphragmatic and quadriceps muscles by ultrasound.

As regards the change in DTe in both CMV and PSV, our study showed that patients on PS ventilation showed a daily increase as early as Days 2-4 by 1.6 % per day and continued to increase on Days 6-8 by 2%/day, while patients on CMV showed a daily decline as early as Days 02 by 1.1 %/day and continued to decline on Days 2-4 by 1.7%/day.

Regarding DTi, our study showed that patients on PSV showed a daily increase on Days 2-4 by 0.1%/day and continued to increase on Days 6-8 by 0.3%/day, while patients on CMV had a daily decrease as early as Days 0-2 by 0.9%/day and continued to decrease on Days 6-8 by 4.5%/day.

Our results were concordant with Elmorsy A. A et al., 2015 [25] stated that patients on PSV showed a daily increase of 1.6%/day starting from day 0 until a mean of 7.23±2.39 days, while patients on CMV had a daily decrease of 3.8%/day from day 0 until a mean of 7.23±2.39 days. Francis et al., 2013 [26] also showed that patients on PSV showed a daily increase of 1.5%/day starting from day 0 of MV until a mean of 5.5±4.3 days, while patients on CMV had a daily decrease of 4.7% / day starting from day 0 and continued over 4.5±4.4 days.

Schepens et al., [27] stated that DTe severely declined on CMV by 9% on Day 0, 11% on day 1, and 6% on Day 2 until a total of starting from day 0 until they were shifted to PSV or underwent tracheostomy (within a mean of 8 days) which high lightening the rapid progression of the diaphragmatic atrophy. The more significant percentages of diaphragmatic decline with Schepens and co-workers may be due to the liberal use of sedation neuromuscular blocking agents during the first 72 hours in contrast to our study, where we excluded any patient on neuromuscular blocking agents).

Horiana et al., [28] stated that there was a daily decline of the diaphragmatic thickness by 6%/day on CMV starting from Days 0-2 and continued over a mean of 5±2 days. Horiana et al. [28] may have obtained more significant percentages of DT atrophy as the study included patients with asthma and COPD who may have dynamic hyperinflation and auto-PEEP during MV that may affect DT measurements, in addition to the small sample size of their study (7 patients).

Regarding changes in DTF on CMV, it showed a daily decline on Days 0-2 by 13%/day and continued on Days 4-6 by 7.1%/day, while patients on PSV showed a daily increase on Days 0-2 by 15% /day, on days 6-8 by 6.7%/day and continued to increase on days 8-10 by 8%/day. Our results were concordant with ER Ali et al. [29], who showed that patients on CMV significantly declined DTF on days 0-3 by 10%/day and on days 4-7 by 6.7% /day. The changes in DTF occur as early as day 0 of invasive mechanical ventilation.

Our study showed that DTF on days 0, 2, and 8 was greater among patients with successful weaning thanthose with failed weaning. In the same context, Farghaly et al. [29] stated that DTF was higher in the successful extubation group (58.9%) compared to the failed one (30.8%).

Regarding weaning from mechanical ventilation, our results showed that the cut-off point of DTF for successful weaning from mechanical ventilation was 33%. Previous studies showed variable cut-off points starting from 30% by Di Nino et al. [30], 234.2% by Farghaly et al. [29], >36% by Ferrari et al. [31], and >40% by Army et al. [32]. Differences in DTF cut-off values may be due to differences in time and technique of measurements, different patient populations, and different durations on MV. Regarding the timing of measurement: In our study, measurements were taken during SBT immediately before extubation, similar to the studies by Farghaly et al. [29] and Ferrari et al. 2014 while the study by Di Ninoet al. [30], the measurements were taken 12-36 hours before extubation.

Regarding lung volumes, DTi and DTe were measured during quiet tidal breathing as in the study by Farghaly et al. [29] while in the study by Agmy et al. [32], DTi was measured at total lung capacity (TLC) and DTe at residual volume (RV). The average duration of ventilatory days in our study was 6.62±3.75 days. At the same time, it was five days in the study by Farghaly et a1. [29], five days in the study by DiNino et al. 2014 [30], seven days in the study by Agmy et al. [32], and 26±2 days in the study by Ferrari et al. [31].

Regarding DTF among different causes of mechanical ventilation, our study showed that DTF on Day 6 was highest among patients with cardiac diseases, followed by parenchymatous lung diseases, then neurological causes, and it was lowest among patients with airway diseases. While ER Ali et al. [33] stated that pneumonia and sepsis worsened DTF, in COPD, a lower percentage of diaphragmatic dysfunction had occurred among this group.

DE was higher on days 2 and 8 among patients with successful weaning than failed weaning. Our results were concordant with Carrie et al. [34], who stated that mean values of DE measured during SBT were higher in patients who succeeded in the weaning attempt when compared to patients with failed waning. Farghaly et al. [29] stated that DE was higher among successful versus failed weaning patients during the SBT. Our study was also concordant with Nassar YS et al. [35], who stated that median DE was higher in successfully weaned vs. failed weaning subjects.

This study showed a cut-off point of DE that can predict successful weaning 19mm at the end of inspiration. Variable cut-off points were mentioned in different studies as >10mm by Kim et al. [19], >10mm by Osman et al. [36], 10.5mm by Farghaly et al. [29], >14mm by Nassar YS et al. 2018 [35], >15mm by ER Ali et al. [33] and up to >25mm by Lerolle et al. [37]. Different results of DE may be explained by the difference in time and technique of measurements. Regarding the timing of measurements: Our measurements were taken before extubation as studies by ER Ali et a1. [33], Nassar YS et al. [35] and Kim et al., while the study by Osman et al. [36] the measurements were recorded after extubation. As regards patient position: in our study, the patients were in a supine position and the head of the bed at zero level. Supine position has been shown to have a lower overall variability, lower side-to-side variability, and more excellent reproducibility [19,37]. Houston et al. [38] compared DE measurements during supine and seated positions for the same patient and found the average value of DE in the supine position allowed greater mobility of the diaphragm (18mm) while in the sitting position allowed lesser mobility of the diaphragm (15.1 mm), Alvarez et al. [39] metanalysis suggested a lower DE accuracy than DTF in predicting weaning outcomes. In patients undergoing MV, DTF reflects active diaphragm contractions without any contribution from the ventilator. At the same time, DE reflects muscle movement that can come from adding patients' respiratory effort and can also be a movement resulting from ventilator lung inflation. Hence, its use is only meaningful in the absence of ventilatory support.

This study found a daily decline in quadriceps thickness as early as days 0-2 by 2.2%/day and on days 8-10 by 1.3%/day. Our results were concordant with Gerovasili et al. [40], which showed that the rate of decline was 2%/day starting from Daly and the second assessment on Day 8. Francis et al. [26] showed a mean decline in quadriceps thickness by 2.0±2.7% per day for all patients (on both PSV and CMV) over a mean period of 7.1±4,7 days starting from Day 0. Also, El Morsyet al. [25] showed a decrease in quadriceps thickness was 3.44% per day for 7.23±2.39 days in both PSV and CMV starting from Day 0.

Our study showed no statistically significant correlation between quadriceps thickness and DTF or DE. In the same context, Vivier et al. [41] and Jung et al. [42] showed no significant correlation between DTF (measured by ultrasound) and quadriceps weakness (assessed by Medical Research Council (NRC) score.

Conclusion:

Successfully-weaned patients showed a daily increase in DTF mean values on days 6-8, while failed-to-wean patients showed a daily decrease in DTF on days 6-10. A cut-off point of 0.33, DTF was associated with successful weaning of the mechanical ventilator.

Successfully weaned patients showed a daily increase in DE mean values on days 0-2 and 8-10 compared to failed-to-wean patients who exhibited a daily decrease of DE on days 6-8. A cut of point 19mm was associated with successful weaning.

Due to the quick onset of diaphragmatic dysfunction in ventilated patients, muscle protection may be needed as soon as possible. Prolonged periods of complete diaphragmatic rest should be avoided and diaphragmatic contraction preserved whenever possible, and respiratory muscle training may improve weaning success.

Due to the apparent decline in diaphragm thickness seen in patients on CMV and the increase in diaphragm thickness seen in all other patients following the institution of PS ventilation, it may be reasonable to assume an early switch from CMV to PS ventilation or even allowing for short periods of spontaneous breathing.

Diaphragmatic ultrasound is a valuable bed side tool to evaluate the diaphragmatic thickness and dysfunction as well as peripheral muscle atrophy in mechanically ventilated patients for a successful weaning process from mechanical ventilation.

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التقييم المستمر لسمك الحجاب الحاجز والعضلات الطرفية باستخدام الموجات الفوق صوتية وتأثيرها على الفطام من جهاز التنفس الصناعى

إن اعتلال الحجاب الحاجز الناتج عن استخدام جهاز التنفس الصناعى يشغل نصيباً كبيراً فى البحث العلمى، وذلك يرجع إلى أن أربعين بالمئة من مرضى العناية المركزة يتاجون إلى جهاز التنفس الصناعى، كما ثبت أيضاً أن حوالى خمسة وعشرون بالمئة يعانون من صعوبة الفطام منه.

ومن المثبت الان أن الموجات فوق الصوتية تعطى معلومات موثقة عن ضمور الحجاب الحاجز بقياس سمكه، وعن الاعتلال الوظيفى له بقياس قوة، شكل وسرعة حركة الحجاب الحاجز، وكما يتميز سهولة استخدامه وتنقله لمرضى العناية المركزة الذين يصعب نقلهم خارج وحدة العناية المركزة.

اشتملت الدراسة على خمسين مريضاً من الذين يحتاجون جهاز التنفس الصناعى وتم تقييم الحجاب الحاجز باستخدام الموجات فوق الصوتية ومتابعة ما إذا تم فطام المريض من جهاز التنفس الصناعى وربط ذلك بسمك الحجاب الحاجز ومعدل حركته كما أن الموجات فوق الصوتية يمكن استخدامها لتقييم سمك العضلات الطرفية ومتابعة ضمورها الناتج عن الإقامة بالعناية المركزة.